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Applicant:	Danishefsky *et al.*	Examiner:	Ungar, S.
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For:	*Colon Cancer KH-1 and N3 Antigens*		

BOX PATENT APPLICATION
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Sir:

REPLACEMENT PARAGRAPH AND PAGES 14-16

Replacement paragraph for the paragraph found at page 1, lines 6-12:

This application is a divisional application filed under 37 C.F.R. § 1.53(b) of application number 09/042,280, filed January 13, 1998, which further claims priority under 35 U.S.C. § 119(e) to U.S. Provisional Application Serial No. 60/034,950, filed January 13, 1997, and the entire contents of each of these applications are hereby incorporated by reference into this application. This invention was made with government support under grants CA-28824-18, GM-15240-02, GM-16291-01, HL-25848-14 and AI-16943 from the National Institutes of Health. Additionally, the present invention was supported in part by a fellowship from the United States Army to Hyun Jin Kim (DAMD 17-97-1-7119). Accordingly, the U.S. Government has certain rights in the invention.

Brief Description of the Drawings

Figure 1 shows the structure of the cell surface antigen KH-1 ceramide and its bioconjugateable O-allyl ether form.

Figures 2(A) and 2(B) provide synthetic Scheme 1. Reagents: (a) (i) 3,3-dimethyldioxirane, CH_2Cl_2; (ii) **4** or **5**, ZnCl2 THF 65% for **6** 55% for **7**; (b) (i) TESOTf, Et_3N, DMAP, CH_2Cl_2, 92%, (ii) $I(coll)_2ClO_4$, $PhSO_2NH_2$, 4 Å molecular sieves, CH_2Cl2, > 90%; (iii) LHMDS, EtSH, DMF > 90%, (iii) LHMDS, EtSH, DMF (iv) Ac_2O, Et_3N, DMAP, CH_2Cl_2, 85%; (d) K_2CO_3, MeOH 80%; (e) (i) MeOTf, di-t-butylpyridine, Et_2O:CH_2Cl_2 (2:1), 4 Å MS (55%), (ii) K_2CO_3, MeOH (85%); (f) (i) MeOTf, di-t-butylpyridine, Et_2O:CH_2Cl_2 (2:1), 4 Å MS (60%); (ii) Ac_2O, Py, DMAP, CH_2Cl_2 (95%); (g) TBAF:AcOH (93%).

Figures 3(A) and 3(B) provide synthetic Scheme 2. Reagents (a) **14**, $Sn(OTf)_2$, Tol:THF (10:1), 4 Å MS (60%); (b) (i) 3,3-dimethyldioxirane, CH_2Cl_2; (ii) EtSH, CH_2Cl_2, H^+ (cat); (iii) Ac_2O, Py, CH_2Cl_2 60% (3 steps) (c) **17** , MeOTf, Et_2O:CH_2Cl_2 (2:1), 4 Å MS (55%); (d) (i) Lindlar's catalyst, H_2, palmitic anhydride, EtOAc, 85% (ii) Na, NH_3, THF; (MeOH quench); (iii) Ac_2O, Et_2N, DMAP, CH_2Cl_2 (iv) MeONa, MeOH, 70% (3 steps); (e) (i) Na, NH_3, THF; (MeOH quench); (ii) Ac_2O, Et_3N, DMAP, CH_2Cl_2; (iii) 3,3-dimethyldioxirane, CH_2Cl_2; (iv) Allyl Alcohol (v) MeONa, MeOH, 60%.

Figure 4 provides a synthetic strategy for N3 antigen.

Figures 5(A), 5(B) and 5(C) provide a synthetic strategy for the Le x donor portion.

Figures 6(A), 6(B) and 6(C) provide a synthetic strategy for the Le a donor portion.

Figures 7(A) and 7(B) provide a synthetic strategy for the N3 acceptor portion.

Figure 8 provides a 2 + 2 coupling for the major N3 antigen.

Figures 9(A) and 9(B) provide a 2 + 4 and 1+ 1 coupling for the N3 antigen.

Figures 10(A) and 10(B) provide a pathway for deprotection of the major N3 epitope.

Figures 11(A) and 11(B) provide a synthetic strategy for the KH-1 tetrasaccharide and hexasaccharide intermediates.

Figures 12(A) and 12(B) illustrate the direct coupling of KH-1 to KLH.

Figures 13(A) and 13(B) illustrate the coupling of KH-1 to KLH via a M_2 cross-linker.